Treatment and Short-Term Follow-up of Symptomatic Atherosclerotic Intracranial Artery Stenosis by Stent-Assisted Angioplasty

MIAO ZHONGRONG LING FENG*, LI SHENGMAO, ZHU FENGSHUI, HUA YANG, WANG MOLI

Department of Neurosurgery*, Center of Diagnostic and Therapeutic Intervention; XuanWu Hospital, Capital University of Medical Science (CUMS); E-mail: Zhongrongm@Yahoo.com

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Summary

Atherosclerotic intracranial artery stenosis can cause hypoperfusion of brain tissues and embolus formation, causing stroke. Conservative medical treatment seemed to have little effect on the natural history and prevent the stroke attack caused by artery stenosis. The purpose of stent-assisted angioplasty is to reconstruct the damaged vessels: the indications, feasibility, effectiveness, complications and follow-up for this new treatment method are discussed.

A series of 32 cases with symptomatic intracranial artery stenosis were accepted from 1998 to 2002. The mean age was 42 yrs (31~76 yr), male/female ratio=23/9. All patients were refractory to optimal medical therapy. Lesions included 12 middle cerebral arteries (37.5%), six basilar arteries (18.75%), three distal ICAs (9.38%) and 12 intracranial Vas (37.5%). All patients were treated by methods of transluminal stent-assisted angioplasty under general anesthesia. Patients were premedicated with Aspirin (300mg/per day) and Ticlopidine (250mg/per day), this was continued for six weeks after the procedure. Medical history, anamnesis, and treatment protocol were reviewed and evaluated retrospectively, short-term follow-up (2mths ~ 1 yr) was also obtained.

Primary clinical presentations were TIAs (21/32, 65.63%), minor stroke (8/32, 25%) and severe stroke (3/32, 9.38%). 31 cases (96.86%) were successfully implanted with coronary stents

within the stenosed vessels; technical success rate was 96.86%. Instant angiographic results showed the stenosed extent had decreased from $72.36\% \pm 5.69$ to $10.16\% \pm 6.94$. One vessel ruptured during the procedure, the patient recovered after surgical repair of the ruptured vessel. Clinical follow-up demonstrated symptoms resolved in most patients (30/32, 93.75%) within the follow-up period, two cases with MCA stenosis had TIAs within two months after the procedure. 12 cases accepted angiographic follow-up. Velocities of stented vessels of five cases (5/21, 23.81%) increased compared to instant results, suggesting restenosis, three of them were confirmed by angiography which included two cases with MCA stenosis (figure 3) and one with distal VA, one of the five cases had recurrent TIAs.

With the newer generation of coronary stent, this technique seemed safe, feasible and effective to prevent stroke attack, but the indication is very important for the technical success. Restenosis remains a common problem as with coronary stenting. Long-term follow-up will be needed.

Introduction

Despite optimal medical therapy, the prognosis for patients with symptomatic intracranial atherosclerotic stenosis is unfavorable. Surgical revascularization may be the option for

Figure 1 A-G. A 42-year-old right-handed man suffered recurrent right-sided weakness and aphasia within 2 weeks. CT scan showed no hemorrhage or ischemic lesions. Acute MRI showed local infarction areas at the left hemisphere (A). TCD suggested high stenosis of the left M1 segment (325 cm/s), the patient was admitted and given appropriate medical therapy. SPECT showed ipsilateral hemispheric hypoperfusion areas (B). Angiogram confirmed high stenosis of the left M1 segment (C, >80%). Stent-assisted angioplasty was performed, a 2.5 x 8 mm coronary stent was deployed at the stenosis site by slowly inflating the balloon to 6 atm (D, E), post-procedure control angiography showed stenosis was dilated to 80% of normal vessel. SPECT 4 days after the procedure showed perfusion restored to nearly normal (F). Eight months angiographic follow-up revealed good patency (G).

the treatment of this disease, but it is a technically demanding procedure that may be accompanied by significant morbidity and mortality. Percutaneous balloon angioplasty has been used to treat intracranial atherosclerotic arterial stenoses. But increased risk of stroke resulting from distal embolization, vessel dissection, acute closure, perforation, arterial rupture or restenosis mean the technique remains uncertain. Stent-assisted angioplasty can provide a favorable clinical course and improved cerebral perfusion and metabolism for patients with symptomatic intracranial artery stenosis.

Compared to coronary arteries, the cerebral arteries within the subarachnoid space represent an interventional challenge. Since 1999, several reports on elective stenting of atherosclerotic lesions of the intracranial arteries using newer, more flexible coronary stents have been published, but most of the series concerned the posterior circulation. We report the experience of 32 patients with symptomatic atherosclerotic intracranial arteries stenosis, treated by stent-assisted angioplasty. The initial experience of this technique is discussed.

Methods

Patients Demographics

Between May 2001 and August 2002, 32 patients with symptomatic intracranial artery stenosis were treated by stent-assisted angioplasty at our center. The mean age was 42 yrs (31 ~ 76 yrs), male/female=23/9. Main risk factors for cerebral infarction included hypertension (n=19), hyperlipidemia (n=16), diabetes (n=14) and coronary heart diseases (n=8). All the patients were treated by the method of direct percutaneous transluminal stent-assisted angioplasty under general anesthesia.

General evaluation pre-treatment

All patients were clinically examined by two experienced neurologists. Patients were given appropriate medical therapy (antiplatelet, anticoagulation, or antifibrinolytic drugs) after hospital admission. CT, MRI and/or MRA, TCD, super sonography, and SPECT were obtained the first week, if the MRA or TCD suggested related artery stenosis, it was decided to perform DSA after permission from the patient and relatives. All the information was then discussed by a group of specialists including interventionists, neurologists, radiologists and neurosurgeons. The degree of stenosis was calculated in relation to the adjacent distal normal vessel diameter (analogous to the method of the North American Symptomatic Carotid Endarterectomy Trial for grading carotid stenosis), and calibration of the measurements was performed with a calibrated stainless steel ball used as the reference.

Indications for stent-assisted angioplasty

Patients referred for the stent-assisted angioplasty had to fulfil the following criteria:

1. Patients were refractory to medical therapy or stable after appropriate therapy but with related artery stenosis > 70%;
2. No severe neurological dysfunction such as complete hemiplegia, coma, or large scale infarction lesions on CT or MRI;
3. If the stenosis degree of symptomatic related artery was >50% but <70%, SPECT must showed ipsilateral hypoperfusion for anterior circulation, or contralateral VA occlusion for

posterior/hypoplasia for bilateral posterior communicating arteries;

4. No severe systemic diseases such as heart failure, renal failure, etc.;
5. Lesioned vessels must be Mori's A or B types;
6. At least three weeks after acute stroke.

Stent-assisted angioplasty technique

Patients were premedicated with high dosage of antiplatelet drugs, Aspirin (300mg/per day) plus ticlodipine hydrochloride (250 mg/per day) for three to four days. All procedures were performed with patients under general anesthesia. Heparinization was given transvenously during the procedure to an activated clotting time (ACT) of 250 ~ 300 seconds. Percutaneous access was obtained via the femoral artery, a 6F catheter sheath was introduced, through which a 100-cm 6F guiding catheter (Cordis Envoy, Cordis Endovascular Systems, Miami Lakes, FL) was navigated. The tip of the catheter rested in the petrosal segment of the ipsilateral ICA for anterior lesions and in the cervical portion of the vertebral artery for posterior lesions. A 0.014-inch floppy-tipped exchange support wire (Luge, Sci Med, Inc) was navigated across the stenosis carefully under road-mapping to permit placement of the stent at the site of the stenosis, the tip of the microwire was advanced into one of the distal branches of the lesion artery. Two kinds of flexible coronary stents were selected, AVE gxf (n=26,) and Helistent (n=5), the length and diameter of the selected stent was determined by the length and the anatomic site of the stenosis, the length of the stent was longer than the actual stenosis length by about 1~2mm, the diameter must be equal to or slightly less than the diameter of the normal vessel and stent must be confirmed to completely cover the stenosis segment. The stents were deployed by last inflating the balloon to 6~7 atm for AVE stent and 5~6 atm for Helistent stent. Pressures were increased to 4~5 atm slowly and slowly about 30 to 60 seconds for the first time, then deflating the balloon to repeat, increasing the pressure to 6~7 atm to ensure full deployment of the stent. Instant angiography was given with the deflated balloon and microguide wire in place. The deflated balloon and microguide wire were gently and carefully pulled out when the stent was confirmed fully expanded and the vessel kept patent. Repeat angiography was given to evaluate the instant dilated result.

Figure 2 A-E A 46-year-old man complained of severe dizziness and dystaxia for about one month, symptoms worsened despite appropriate medical therapy. He had a ten year history of coronary disease and accepted PTCA once, MRI showed bilateral infarction lesions at the brain stem (A). Angiogram showed his right VA occluded and a high stenosis lesion at the proximal portion of BA (B, C, >90%) and absence of right PCA, his bilateral posterior communicating arteries were dysplastic. A 3.0 x12 mm coronary stent was deployed at 7 atm, instant angiography showed the vessel was dilated to about 80% of normal diameter, right PCA presented according to the increased blood perfusion. The patient recovered five month after the procedure.

Patients were awakened immediately after the procedure, each patient underwent a complete neurologic examination, after which they were monitored for 72 hours in ICU. Heparin metabolized naturally. A high dosage of antiplatelet

drugs continued for at least six weeks after procedure if there was no systemic hemorrhagic complication.

Repeated SPECT and TCD were given within one week after successful stenting.

Figure 3 A 54-year-old man, admitted with recurrent left arm weakness for two days. MRI showed a small infarction lesion at the right basal ganglion (A), SPECT showed ipsilateral hemispheric hypoperfusion areas, angiogram found high stenosis (>80%) at the right M1 segment (B). A coronary stent was deployed at the stenosis site (C) and fully dilated the stenotic vessel (D), local blood perfusion improved as confirmed by SPECT ten days after the procedure. Symptoms resolved after the procedure: seven month follow-up showed restenosis within the stent, but the patient referred no symptoms (E).

Follow-up

The time between angioplasty and the last follow-up examination ranged from two to 11 months (mean, four months). Five patients were lost to follow-up, the remaining 26 patients underwent follow-up neurologic examination: 21 (80.77%) had TCD follow-up, 12 (38.71%) had DSA.

Results

Primary clinical presentations were TIAs (22/32, 68.75%), minor stroke (8/32, 25%) and

severe stroke (2/32, 6.25%). Lesions included middle cerebral arteries (n=12, 37.5%), basilar arteries (n=6, 18.75%), distal ICAs (n=3, 9.38%) and intracranial VAs (n=12, 37.5%). SPECT showed 14 cases (14/15) of anterior circulation with ipsilateral hemispheric hypoperfusion areas; of these, ten cases (10/14, 71.43%) improved immediately after angioplasty (figures 1 and 2). TCD suggested that the velocities at the stenosis site decreased from 324 ± 23 cm/s to 146 ± 18 cm/s.

31 cases were successfully implanted coronary stents within the stenosed vessels, techni-

Figure 4 42-year-old woman complained of recurrent right arm weakness for one month. She was refractory to medical therapy and had no risk factors for cerebral ischemia. MRI showed a small infarction area at the left basal ganglion. Angiogram showed high grade left M1 segment stenosis from the proximal to distal portion (A), >90%). The patient underwent stent-assisted angioplasty. Unfortunately, angiography showed the vessel ruptured as soon as the stent reached its destination (B), a stent was deployed and the balloon was kept dilated to occlude the ruptured vessel, the patient was changed to emergency surgical operation and an acute craniotomy was done. The ruptured point was found and homeostasis undertaken with spongy cotton and glue (NBCA). The balloon and microguide wire were pulled out after completely repairing the vessel. It was astonishing that the patient awoke four hours after the operation with no neurological dysfunction. Angiogram showed the left M1 segment occluded one month later, but there were collaterals from ipsilateral ACA and PCA (D-E). She had no symptoms at one year follow-up (F).

cal success rate was 96.86%. Instant angiographic results showed the stenosed extent was decreased from $72.36\% \pm 5.69$ to $10.16\% \pm 6.94$ (figures 1 and 2). One case with MCA stenosis had severe complications during the procedure, vessels ruptured during the procedure, fortunately, the patient recovered after surgical repair of the ruptured vessel (figure 4).

Clinical follow-up showed that most of them (24/26, 92.31%) improved with no stroke attack

within the follow-up period, two cases with MCA stenosis had TIAs within two months after the procedure. 21 (80.77%) had TCD follow-up. Velocities at the stented vessels of five cases (5/21, 23.81%) increased compared to instant results. This may suggest restenosis: three of them were confirmed by angiography which included two cases with MCA stenosis (figure 3) and one with distal VA stenosis, one of the five cases had recurrent TIAs.

E

F

Discussion

Hemodynamic insufficiency and intra-arterial embolization due to arterial stenotic-occlusive disease are possible causes of cerebral ischemia. In the study by Craig et al.², 58 patients with intracranial ICA stenosis were followed. At the end of the 30-month follow-up period, only 33% were alive and free of subsequent cerebrovascular events. Of the patients studied, 43% died during follow-up; 36% of these deaths were because of stroke. The risk of stroke in patients who harbor a stenosis of greater than 50% in the intracranial vertebrobasilar artery system have a risk of stroke 17 times greater than in the matched normal population²¹. Despite best current medical efforts, stroke rates for symptomatic patients with intracranial artery stenosis remain high. Medical therapy for chronic anterior intracranial artery stenosis was also unsatisfactory. The Warfarin-Aspirin Symptomatic Intracranial Disease Group has reported on the outcome for medically managed patients with 50 to 99% stenosis of the intracranial vertebral artery and basilar artery³². Of 68 patients treated with aspirin or warfarin, 22% of them suffered a stroke at a median follow up of 13.8 months. In addition, seven (16%) of 42 patients treated with warfarin sustained a hemorrhagic complication, and two of them died. A retrospective

study showed that 35.24% patients (86/244) with symptomatic cerebral ischemia harbored related intracranial artery stenosis in our hospital (unpublished data), 34 of the 86 cases (39.53%) had secondary stroke despite appropriate medical therapy.

Balloon angioplasty has been performed as an adjunct to the medical management of intracranial atherosclerotic disease^{13,15,16,23,29,33}. However, the complication rate of 7%~38% according to different reports limited its widespread use; Complications include plaque/vessel recoil, vessel dissection, and acute vessel occlusion secondary to dissection or platelet aggregation. Although recent experience suggests that there have been significant improvements in technique and materials, the impact of balloon angioplasty on the degree of stenosis is minimal, and most patients continue to be treated with warfarin after the procedure.

Stent-assisted angioplasty has become an effective technique to prevent tissue ischemia with artery occlusive diseases of coronary, iliac, and other peripheral vasculature, this technique has also obtained satisfactory results in extracranial arteries such as proximal ICA or proximal VA^{3,4,9,24,29}. After Phatouros et al²⁵ first reported successful stenting for basilar artery thrombosis in 1999, several reports have published encouraging results concerning the clinical application of stent placement for in-

tracranial artery stenosis. Gomez et al.⁸ reported a series of 12 symptomatic patients with basilar artery stenosis who underwent stent-assisted angioplasty. Stent placement was successful in all patients with significant changes in the degree of stenosis from 71.4% to 10.3. Clinical follow-up was available for 0.5 to 16 months: only one patient had a transient ischemic attack. Mori et al.²⁰ reported ten patients with 12 intracranial atherosclerotic lesions of the vertebrobasilar artery and the distal internal carotid artery who underwent treatment with flexible balloon-expandable coronary stents. In two of the ten patients the procedure was not successful because of the inability to access the site of arterial stenosis. Ten lesions in eight patients were successfully dilated with stents, no complications occurred during or after the procedure and no neurologic ischemic events or restenoses occurred during the follow-up period. However, most of these reports concerned the posterior circulation, the reason may be the relatively less tortuous posterior angioarchitecture, the case report by Gomez et al [7] may be the only report of elective stenting for the symptomatic middle cerebral artery, they deployed a stent in a stenosis MCA after successful thrombolysis.

Considering the tortuous configuration of the intracranial arteries, almost all the authors emphasized the indications for stenting^{7,8,12,13,14,15,16}. One of the most important factors is the condition of the stenosed vessel: those belonging to Mori's B or C type are dangerous for stenting. One of our patients described with MCA stenosis had severe complications because of the stenosed vessel angle: as the stent passed through this site, it became ruptured. Although the patient recovered later it was a very impressive case for us. In addition, highly calcified or long length stenosis are also dangerous for stenting.

The technique of angioplasty and stenting consists of crossing the stenotic lesion with a soft-tip atraumatic and hydrophilic guidewire. Great care should be taken to avoid the wire passing through the real lumen other than a dissection. In addition, perforation of the intracranial artery distal to the lesion by the tip of the wire is another risk. This nearly occurred on two occasions, when the stent across the wire passed through a tortuous segment abruptly, or pulling out the balloon after de-

ployment when the wire remains in place, at this moment, the tip of the wire may "jump" forward when the balloon backs out.

Predilation is very common in extracranial arteries and coronary arteries, Predilation may prepare a route of atraumatic passage for the balloon-mounted stent and reduces the resistance to expansion of the stent during inflation for intracranial arteries, especially in highly stenotic lesions. We did not use balloon predilation for any of our patients. We think predilation may increase the risk of the procedure, for most of the selected coronary stents, it has a soft thin tip to ensure safety passing through the stenosis segment across the wire.

The rate and extent of balloon inflation during the procedure was important. All inflations must be made very slowly, because slow inflation and stretching of the vessel may allow the viscoelastic qualities of the vessel wall to accommodate the slow expansion of balloon-mounted stent rather than force the wall to crack abruptly. For most of the coronary stents, during inflation the balloon is designed to expand initially at the distal and proximal ends and then in the center section containing the stent. Quick expansion of these two ends may cause vessel rupture at these two points. The sustained, low-pressure inflation can sometimes be repeated one to two times and the stents eventually distended to full diameter. Occlusion of the ostia of the lenticulostriate branches perforating arteries of the brain stem is another potential complication. Although this did not occur in our series, Levy et al¹³ reported one series of patients in which one case with basal artery stenting developed brain stem infarction. The author attributed this to occlusion of the ostia of the perforated vessel. Lanzino et al.¹² found if the strut of stent covers 50% of the ostia of the lenticulostriate branches it can be kept open.

The gfx and helistent coronary stents, which had good flexibility and are of an appropriate length to follow arterial tortuosity, can be made to conform to vascular morphology. We did not fail to deploy a stent to the lesion site and succeeded in all cases even in several cases of MCA stenosis with tortuous siphon. In this situation, we gave a stable strength to the stent and gently pulled out the wire, or sometimes we pushed the stent and the wire together little by little. For very difficult cases, we navigated the guiding

catheter as far as possible to support the stent, in two of our cases, the tip of the guiding catheter reached the cavernous segment (C4).

Pharmacological preparation of a patient undergoing an elective stenting procedure for an intracranial atherosclerotic lesion is crucial. Much like in coronary stenting, pretreatment with platelet inhibitors such as Acetyl Salicylic Acid (ASA), Ticlopidine or Clopidogrel is mandatory to successfully maintain the patency of the artery after deploying a stent. Failure to pretreat the patient with antiplatelet agents predisposes to acute or subacute thrombosis of the stent, particularly when deployed in small arteries. During the stenting procedure, an adequate level of anticoagulation with Heparin is necessary to prevent thrombo-embolic complications. Medication with strong antiplatelet drugs after the procedure must be continued to prevent aggregation of platelets and acute/sub-acute thrombosis.

Evaluation of a successful procedure includes vessel patency, clinical improvement, cerebral perfusion and restenosis. In our series, 31 cases were successfully implanted with coronary stents within the stenosed vessels: the technical success rate was 96.86%. Instant results showed the stenosed extent was decreased from $72.36\% \pm 5.69$ to $10.16\% \pm 6.94$. To improve cerebral perfusion and metabolism, stent-assisted angioplasty is as effective as the STA-superior cerebellar artery by-pass procedure (Uchiyama et al, 2001). SPECT demonstrated

improved blood perfusion in ten cases (10/14, 71.43%) after angioplasty. TCD suggested that the velocities at the stenosis site decreased from 324 ± 23 cm/s to 146 ± 18 cm/s.

The purpose of angioplasty is to reconstruct the vascular passage and to improve cerebral perfusion and metabolism. Clinical follow-up showed that most of our patients (24/26, 92.31%) improved and no stroke attack occurred within the follow-up period. Only two patients with MCA stenosis had TIAs within two months after the procedure.

Restenosis after angioplasty is another interesting topic after angioplasty^{13,23,26,29} in our series. The restenosis rate in studies reported in the literature ranges from 0% to 25% after angioplasty of a vessel in the posterior circulation and as high as 36% after angioplasty of a vessel in the anterior circulation³³. Velocities at the stented vessels of five cases (5/21, 23.81%) increased compared to instant results, suggesting restenosis. Three of them were confirmed by angiography which included two cases with MCA stenosis and one with distal VA stenosis, one of the five cases had recurrent TIAs. It may be suggested that the smaller the vessel, the more likely restenosis will occur.

Conclusion

Long-term follow-up data and additional clinical experience are required to assess the durability of this approach.

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Dr Miao Zhongrong Ling Feng
 Department of Neurosurgery
 Center of Diagnostic and Therapeutic Intervention
 XuanWu Hospital
 Capital University of Medical Science (CUMS)
 E-mail: Zhongrongm@Yahoo.com